Otezla

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/07/2022		PL	
II/0038	C.I.13 - Submission of the final study report (CSR) from PsOBest Registry, listed as a category 3 study in the RMP. This is an observational study to assess	05/05/2022	n/a		n/a

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	the long-term safety and effectiveness of apremilast in routine clinical practice in Germany. The RMP version 14.1 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0039	C.I.13- Submission of the final study report (CSR) from UK Clinical Practice Research Database (CPRD), listed as a category 3 study in the RMP. This is an observational study to assess the long-term data of apremilast in patients with psoriasis and psoriatic arthritis. The RMP version 14.1 is accepted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	07/04/2022	n/a		This variation concerns the final study reports of the post-authorization safety study "Clinical Practice Research Datalink (CPRD) data analysis for psoriatic arthritis and psoriasis", listed as a category 3 study in the Risk Management Plan (RMP), to evaluate the risk of Adverse Events Special Interest (AESIs) in patients exposed to apremilast compared to a set of patients with psoriasis or psoriatic arthritis who received other treatments. Overall, the results do not suggest any new safety concerns for Apremilast and are in line with the known safety profile. However, the study has several limitations concerning quality and completeness of data from CPRD Aurum, low sample size, and unadjusted study outcomes that do not allow to reach robust conclusions.
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/07/2021		PL	
IAIN/0036/G	This was an application for a group of variations. B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.b.1.b - Replacement or addition of a	30/04/2021	n/a		

	manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IB/0034/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	14/04/2021	21/06/2021	Annex II and PL	
IAIN/0033/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer	24/06/2020	21/06/2021	Annex II and PL	

	responsible for importation and/or batch release - Not including batch control/testing				
II/0029	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	27/02/2020	08/04/2020	SmPC and PL	Please refer to Scientific Discussion Otezla - EMEA/H/C/003746 -II-0029
T/0032	Transfer of Marketing Authorisation	07/01/2020	31/01/2020	SmPC, Labelling and PL	
IB/0031	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	18/10/2019	31/01/2020	SmPC, Labelling and PL	
PSUSA/10338 /201903	Periodic Safety Update EU Single assessment - apremilast	03/10/2019	n/a		PRAC Recommendation - maintenance
R/0027	Renewal of the marketing authorisation.	27/06/2019	23/08/2019	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Otezla in the approved indications remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/07/2019	31/01/2020	Labelling and PL	
II/0023	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH	14/06/2019	n/a		

	where significant assessment is required				
IA/0026	A.7 - Administrative change - Deletion of manufacturing sites	11/03/2019	23/08/2019	Annex II and PL	
IA/0025	A.7 - Administrative change - Deletion of manufacturing sites	20/02/2019	n/a		
PSUSA/10338 /201803	Periodic Safety Update EU Single assessment - apremilast	18/10/2018	18/12/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)'for PSUSA/10338/201803.
II/0021	Update of sections 4.2 and 5.1 of Otezla SmPC with information up to 5 years of treatment following the long-term extension phases of 2 pivotal Phase 3 studies of apremilast in the treatment of moderate to severe plaque psoriasis and 3 pivotal and 1 supportive Phase 3 studies in the treatment of active psoriatic arthritis (CC-10004-PSA-002, -003, -004, -005 and CC-10004-PSOR-008, - 009) listed as a category 3 study in the RMP (MEA 002) C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	08/11/2018	23/08/2019	SmPC	In psoriatic arthritis patients, ACR responses were maintained in the long-term open label extension studies for up to 5 years. The clinical responses were maintained in the same parameters of peripheral activity and in the skin manifestations of psoriasis in the open-label extension studies for up to 5 years of treatment. Improved physical function as assessed by the HAQ-DI and the SF36v2PF domain, and the FACIT-fatigue scores were maintained in the open-label extension studies for up to 5 years of treatment. In psoriasis patients, improvements were generally maintained in PASI score, affected BSA, itch, nail and quality of life measures for up to 5 years. The long-term safety of apremilast 30 mg twice daily in patients with psoriatic arthritis and psoriasis in open-label extension studies for a total duration of treatment up to 5 years was generally comparable to the 52-week studies.
IAIN/0024/G	This was an application for a group of variations.	18/10/2018	18/12/2018	Annex II and PL	

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information				
T/0020	Transfer of Marketing Authorisation	29/06/2018	02/08/2018	SmPC, Labelling and PL	
IA/0022	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	01/08/2018	n/a		
II/0018	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	08/03/2018	n/a		

II/0017	Update of section 4.4 and 4.8 of the SmPC to include a warning on severe diarrhoea, nausea, and vomiting following a safety cumulative review of all data sources. The PL has been updated accordingly. In addition the MAH took the opportunity to introduce editorial changes in Annex IIIA and to align the PI with QRD template 10.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	09/11/2017	02/08/2018	SmPC, Labelling and PL	The Product Information has been updated with the inclusion of wording in the SmPC to describe that there have been post-marketing reports of severe diarrhoea, nausea, and vomiting associated with the use of Otezla. Most events occurred within the first few weeks of treatment. In some cases, patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications. Patients who reduced dosage or discontinued Otezla generally improved quickly. If patients develop severe diarrhoea, nausea, or vomiting, discontinuation of treatment with apremilast may be necessary
PSUSA/10338 /201703	Periodic Safety Update EU Single assessment - apremilast	28/09/2017	n/a		PRAC Recommendation - maintenance
IB/0015	B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	27/04/2017	n/a		
PSUSA/10338 /201609	Periodic Safety Update EU Single assessment - apremilast	06/04/2017	n/a		PRAC Recommendation - maintenance
IB/0014/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	08/03/2017	n/a		

	re-test period/storage period supported by real time data				
IB/0012	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/12/2016	n/a		
II/0011	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/12/2016	n/a		
PSUSA/10338 /201603	Periodic Safety Update EU Single assessment - apremilast	13/10/2016	08/12/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)'for PSUSA/10338/201603.
PSUSA/10338 /201509	Periodic Safety Update EU Single assessment - apremilast	28/04/2016	08/07/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)'for PSUSA/10338/201509.
IB/0009	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/03/2016	n/a		
IB/0008	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	22/01/2016	08/07/2016	SmPC and PL	
IA/0006/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or	30/10/2015	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size				
PSUSA/10338 /201503	Periodic Safety Update EU Single assessment - apremilast	08/10/2015	n/a		PRAC Recommendation - maintenance
IG/0590	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	22/07/2015	n/a		
II/0003/G	This was an application for a group of variations. Submission of non-clinical studies CC-10004-DMPK-1965 and CC-10004-DMPK-1966 in fulfilment of MEA 001. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/06/2015	n/a		
IB/0002	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/04/2015	n/a		

IA/0001	B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	13/03/2015	n/a		